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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/631,152	08/02/2000	Jon A. Wolff	Mirus.017.01	8109

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EXAMINER
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/631,152	WOLFF ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2004 and 04 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5 and 7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Papers filed 17 September 2004 and 4 October 2004 in response to the Non-Final Office Action mailed 22 March 2004. Claims 18-23 had been withdrawn from consideration and claims 1, 3-5 and 7-16 were considered in the 22 March Office Action. Claims 18-33 were canceled and claims 1, 14, 15 and 16 were amended in the 4 October Paper. Claims 1, 3-5 and 7-16 are pending and under consideration.

Response to Amendment

Claim Rejections - 35 USC § 112

Rejection of claims 1, 3-5 and 7-16 under 35 U.S.C. 112, first paragraph, as lacking adequate written description is withdrawn in view of the amendments to the claims and the showings of the Declaration under 37 CFR §1.132 filed 17 September 2004.

Claims 1, 3-5 and 7-16 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter for reasons of record and herein below in the response to arguments.

Rejection of claims 14-16 under 35 U.S.C. 112, second paragraph, as indefinite is withdrawn in view of the amendments to the claims.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 1, 3-5 and 7-16 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for nucleic acid delivery to a cell *in vitro*, does not reasonably provide enablement for a process for nucleic acid delivery to a cell *in vivo*.

In response to the *prima facie* case and arguments of record, Applicant expresses puzzlement because Examples 3-6 and 8 describe *in vivo* delivery and expression and submits a Declaration under Rule 1.132 allegedly showing additional *in vivo* examples. While agreeing that the claimed process could be used for therapeutic purposes and stating that the method is currently being used for determining amounts and locations of genetic material delivered to various organs, Applicant urges that the specification is not intended to be limited to therapeutic uses.

Declaration under 37 CFR §1.132

The declaration discloses experiments in which nucleic acids encoding reporter genes were labeled with peptide nuclear localization signals and delivered into HeLa cells *in vitro*. Expression of the reporter gene in the cultured cells was then determined. In the Declaration, Applicant concludes, based on the findings of both Examples 1 and 2 that, "this approach was not suitable to increase the overall expression levels by the enhancement of the nuclear entry of pDNA" (page 2, third full paragraph and page 7, first full paragraph).

Applicant's arguments and the showings of the declaration have been fully considered but are not deemed persuasive. With regard to the assertion that the method practiced *in vivo* can

be applied to purposes other than gene therapy, Applicant is again reminded that the enabling specification must teach those skilled in the art to make and use the full scope of the claimed invention without undue experimentation (see the first paragraph on page 7 of the 22 March Office Action). The claims are clearly not limited to research application and, in fact, the teachings of the specification with regard to using the claimed method *in vivo* are almost exclusively focused on therapeutic application. In the paragraph bridging pages 2-3, the specification teaches gene therapy by expression of a whole or partial protein or antisense; on page 3, the specification contemplates gene replacement therapy of Duchenne muscular dystrophy, as well as treatment of neurodegenerative disorders, cancer, heart disease and infections using the claimed invention; and the specification further teaches expression of therapeutic genes such as erythropoietin, FGF and VEGF. Thus, it is clear from the disclosure that the intended use for the claimed method is gene therapy, and that the method is to be used for gene therapy of extremely complicated diseases such as muscular dystrophy, neurodegenerative disorders, cancer and heart disease. Therefore, the specification is plainly teaching that the method is to be used therapeutically.

As stated in the First Office Action on the Merits, "[w]hile it is relatively routine in the gene transfer art to achieve expression at non-therapeutic levels (i.e. levels providing no patentably useful phenotypic effect), the skilled artisan would have to engage in trial and error experimentation to achieve expression of a particular molecule at levels sufficient for therapeutic effect" (16 December 2002 Office Action, paragraph bridging pages 15-16). For reasons provided in previous Office Actions, the working examples cited by Applicant are not demonstrative of an enabled gene therapy. Furthermore, using the method to determine the

amount and location of genetic material delivered to various organs and "therapeutic related experiments" is not a patentable utility. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities and therefore not patentable. MPEP § 2107.01 I. Given the focus of the disclosure of therapeutic use of the claimed method and the absence of an enabled therapy, the reporter gene experiments amount to "carrying out further research" for the purpose of developing the method such that it can be used for therapy as asserted in the specification. This is not a patentable utility.

Finally, in contrast to Applicant's assertion, the experiments disclosed in the Declaration were not performed *in vivo* and, therefore, are clearly not probative of enablement for the method practiced *in vivo*.

Applicant's arguments have been fully considered in view of the record as a whole but are not deemed persuasive. Therefore, the claims stand rejected under 35 USC §112, first paragraph, as lacking enablement for the full scope of the claimed subject matter.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.
Examiner
Art Unit 1636